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ART UNIT	**PAPER NUMBER**
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/870,122	CLEARY ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-98* is/are pending in the application.

4a) Of the above claim(s) *28-59,73,74 and 79-98* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-72 and 75-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *53001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicants' preliminary amendments filed 11/10/03, 05/30/01, 02/27/02, 05/02/02, 03/04/03 and 07/31/03. With these, Applicants have amended the specification.

Election

2) Acknowledgment is made of Applicants' election filed 03/04/03 in response to the restriction requirement mailed 11/12/02. Applicants have elected invention 14, claims 70 and 71, with traverse. Applicants have further elected amino acid 193 under the assumption that this is an election of species. Applicants' traversal is on the grounds that restriction requirement is optional in all cases. Applicants contend that if the search and examination can be made without serious burden, the Office must examine claims to distinct or independent inventions. Applicants further cite MPEP 803.02 and state that if the members of the Markush species are sufficiently few in number or are so closely related that a search and examination of the entire claim can be made without serious burden, all the members of the Markush group in the claim must be examined, even though they are directed to independent and distinct inventions.

Applicants' arguments have been carefully considered. With regard to the amino acid residues, all of the recited residues have been examined. With regard to the inventive groups, as set forth in the restriction requirement mailed 11/12/02, the individual polynucleotides and different SCP peptidase variants are products structurally and/or immunologically distinct from each other and belong to two different classes. The products encompassed in the inventions are structurally distinct from one another, each sequence requiring a separate search. The methods of inventions 15-29 are methods of using the various SCP variants and they also belong to different class/subclass. MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed, and (2) a serious *search and examination* burden is placed on the Examiner if restriction is not required. The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example, as product and method of use, but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (MPEP 802.01). In the instant case, the various products of inventions 1-14 are capable of separate use, i.e., a non-vaccine use as a diagnostic reagent. Applicants have not presented any arguments establishing that the claimed product cannot be used in a materially different non-immunization process. Furthermore, MPEP 803 states that a burden can be shown if the Examiner shows either separate classification, different field of search, **or** separate status in the art. In the instant application, such a burden has been established. Further, it should be noted that the non-patent literature search, particularly in this art, is non-coextensive. Clearly, different searches and issues are involved in the examination of each invention.

For these reasons, the restriction set forth in the Office Action mailed 11/12/02 is proper and is hereby made FINAL.

Status of Claims

3) Claims 1-27 have been canceled via the amendment filed 03/04/03.

Claims 28-98 are pending.

Claims 70 and 71 have been elected.

Claims 28-59, 73, 74 and 79-98 have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Elected claims 70 and 71 and the linking claims 60-69, 72 and 75-78 are under examination. A first action on the merits is issued on these claims.

Sequence Listings

4) Acknowledgment is made of Applicants' submission of CRF and the raw Sequence Listings, which have been entered on 11/14/03 and 12/05/01.

Information Disclosure Statement

5) Acknowledgment is made of Applicants' Information Disclosure Statement filed 05/30/01. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Drawings

6) The drawings submitted in the instant application are not objected to by the Draftsperson under 37 C.F.R 1.84 or 1.152 and as such, the drawings have been approved as formal drawings.

Priority / Continuity

7) The instant application is a Continuation of PCT/US99/28826, filed 12/03/1999, which is a Continuation of application SN 09/206,898, filed 12/07/1998, now US patent 6,355,255, which is a Continuation-in-part of application SN 08/589,756, filed 01/22/1996, now US patent 5,846,547.

Specification

8) The instant specification is objected to for the following reason(s):

(a) The amendment introduced to the first paragraph of the specification to include priority applications contains incorrect information with regard to the numbers of the issued patents. The application SN 09/206,898 is not issued as US patent 5,846,547 and the application SN 08/589,756 is not issued as US patent 6,355,255.

(b) At line 24 on page 32, the address of the American Type Culture Collection is incorrect. Effective 23 March 1998, ATCC has a new address: 10801 University Boulevard, Manassas, VA 20110-2209. Amendment to the specification is suggested to reflect this. It is suggested that Applicants examine the whole specification to make similar correction to the address, wherever it appears.

(c) At lines 24 and 30 respectively on page 8 of the specification, the limitations 'Figure 9.' and 'Figure 10.' should be replaced with --Figure 9A and 9B.-- and --Figure 10A and 10B.--.

(d) The use of the trademarks has been noted in this application. For example, see lines 10 and 12 on page 33: 'Sepharose 6B'; lines 5 and 7 on page 33: 'Sepharose 4..'; line 6 on page 44 and line 26 on page 45: 'Invitrogen'; line 2 on page 43: 'Sequenase' and 'Stratagene'; line 8 on page 23: 'Mutanolysin'; page 34, line 13: 'Eppendorf'; and line 12 on page 20: 'Appligene'. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification and make necessary changes wherever trademark recitations appear.

Rejection(s) under Non-Statutory Double Patenting

9) The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970) and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R 3.73(b).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See e.g., *In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998)*; *In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993)*; *In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir, 1985)*.

10) Claims 60-63, 67, 68, 77 and 78 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 22 and 28 of Cleary (US 6,270,775) ('775). Although the conflicting claims are not identical, they are not patentably distinct from each other, because instant claims 60-63, 67, 68, 77 and 78 are generic to what is recited in the cited claims of US patent 6,270,775. Instant claims are anticipated by the cited claims of US patent 6,270,775.

11) Claims 60, 61, 77 and 78 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of Cleary (US 5,846,547 – Applicants' IDS) ('547). Although the conflicting claims are not identical, they are not patentably distinct from each other, because the SCP claimed in the cited claims of US patent 5,846,547 falls within the scope of instant claims, or in other words, instant claims are anticipated by the cited claims of US patent 5,846,547.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

12) Claims 69-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for the enzymatically inactive SCP variants having the specific amino acid substitutions, i.e., SCPA49D130A; SCPA1D130A; SCPBD130A; SCPA49H193A; SCPA1H193A; SCPBH193A; SCPA49N295A; SCPA1N295A; SCPBN295A; SCPA49512A; SCPA1S512A; and SCPB512A, does not reasonably provide enablement for the large number of enzymatically inactive SCP variant members or species currently encompassed within the scope of the instant claims, having one or more conserved or non-conserved amino acid modification(s) or substitutions at positions 260, 261, 262, 415, 416, 417, 130, 193, 295 or 512, as claimed in a broad sense.

Instant claims are evaluated based on the *Wands* analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant case, the nature of the invention includes modifying or enzymatically inactivating or completely attenuating a wild-type SCP polypeptide by mutation, i.e., modification or substitution, at one or more positions of 260, 261, 262, 415, 416, 417, 130, 193, 295 or 512, with one or more conservative or non-conservative amino acids. However, other than the enzymatically inactive specific SCP variants, SCPA49D130A; SCPA1D130A; SCPBD130A; SCPA49H193A; SCPA1H193A; SCPBH193A; SCPA49N295A; SCPA1N295A; SCPBN295A; SCPA49512A; SCPA1S512A; and SCPB512A, the large number of SCP variants concurrently having the recited property or function are neither taught within the instant specification, nor is it predictable to obtain such peptide variants having such a property. Although the relative skill of those in this art is high, the breadth of the claims is unfoundedly broad and encompasses a significant number of SCP variant species whose ability to have the function or property recited, i.e.,

enzymatic inactivity, cannot be predicted following one or more conservative or non-conservative amino acid modification(s) or substitution(s) at one or more of the recited positions. It is important to note that the purpose of the invention is to use the claimed SCP variant as an active ingredient in a vaccine composition. The vaccine application minimally requires a specific interaction of the claimed peptide variant with a specific antibody. In the instant case, the claimed product is a peptide of unlimited size or length, which is required to be enzymatically inactive, while having one or more conservative or non-conservative amino acid substitutions or modifications at one or more of amino acid residues at positions 260, 261, 262, 415, 416, 417, 130, 193, 295 and 512. Encompassed in the scope of the claims are single SCP variants, double variants, triple variants, or variants having multiple amino acid substitutions/modifications at all the ten positions stated above. Although one of skill in the art may be able to make amino acid substitutions, the ability of the resultant peptide variants having multiple conservative or non-conservative amino acid substitutions to be enzymatically inactive and elicit antibodies that would neutralize the wild-type SCP and thus serve as active elements of a vaccine is not predictable. There is no evidentiary support in the specification that an SCP variant with more than one amino acid substitution, if constructed, would be enzymatically inactive and immunogenically functional as a vaccine specifically against streptococci. It should be noted that modifications of a native polypeptide at multiple positions can potentially alter its conformational, antigenic and immunogenic integrity, and the use of such an excessively modified polypeptide as a vaccine would potentially result in a non-effective vaccine. One or more random replacements affecting the epitopic amino acid positions that are critical, for example, to the three-dimensional conformational structure and specific binding property of the protein, would result in a polypeptide that may be non-functional (i.e., non-immunogenic) or not optimally immunogenic as a vaccine candidate, because such positions tolerate no or little modifications. For instance, Houghten *et al.* (New Approaches to Immunization, *Vaccines86*, Cold Spring Harbor Laboratory, p. 21-25, 1986) taught the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten *et al.* state (see page 24):

> One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool.

Thus, the art reflects that variations in critical residues at specific positions in an amino acid sequence could result in a polypeptide, which may induce an antibody that may not recognize or bind to the native polypeptide of a microorganism. In the instant case, this is important because the purpose of the instant invention is to use the claimed SCP variant as a vaccine. The state of the art reflects functional unpredictability with regard to even conservative amino acid replacements within a polypeptide. For

instance, Lazar *et al.* (*Mol. Cellular Biol.* 8: 1247-1252, 1988) demonstrated that a substitution of Leu with a conservative amino acid residue, such as, Ile or His in the transforming growth factor (TGF) alpha led to a mutant protein with dramatically altered biological activities. Lazar *et al.* stated that they "did not expect that a mutation of Leu to Ile (which have similar sizes and polarities) would cause such a strong effect". See paragraph bridging left and right columns on page 1251; and third full paragraph on page 1251. Lazar *et al.* also taught that in transforming growth factor alpha, replacement of aspartic acid at position 47 with a conservative amino acid, glutamic acid, sharply reduced the biological activity of the mitogen. Thus, one simply cannot predict what effects a given deletion, insertion or modification in the sequence would cause, and therefore such modified SCP variant molecules are not enabled as Applicants' invention. Similarly, it has been shown in the art that attenuation of the biological (hemolytic) activity of a wild-type bacterial polypeptide (pneumolysin) by any random mutation is unpredictable. For instance, Feldman *et al.* (*Am. J. Respir. Cell Mol. Biol.* 5: 416-423, 1991) showed that, while a Trp 433 > Phe modification results in a modified pneumolysin having a lowered haemolytic activity, a Tyr 384 > Phe modification results in a modified pneumolysin that had normal hemolytic activity (see page 417). The state of the art clearly suggests that a mutation at any random position does not result in a modified pneumolysin polypeptide with an attenuated hemolytic activity. Mitchell *et al.* (*Mol. Microbiol.* 5: 1883-1888, 1991) showed that individual modifications of Trp 379 and Trp 397 to Phe, or of residues Tyr 384 and Asp 385 to Phe and Asn respectively, did not alter the cytolytic activities of resultant modified pneumolysins (see page 1885, left column). The post-filing state of the art shows that an Asp 385 >Asn mutation in the pneumolysin gene resulted in a modified pneumolysin that retained 100% hemolytic activity of wild-type pneumolysin (see Table 1 of Alexander *et al. Microb. Pathogen.* 24: 167-174, March 1998). Therefore, absent a concrete demonstration, the immunological specificity and the biological activity of a microbial polypeptide variant is not predictable. In the instant application, while the specification is enabling for the specifically disclosed single mutants, SCPA49D130A; SCPA1D130A; SCPBD130A; SCPA49H193A; SCPA1H193A; SCPBH193A; SCPA49N295A; SCPA1N295A; SCPBN295A; SCPA49512A; SCPA1S512A; and SCPB512A pNV207, pNV111, pNV211 and pNV103, it is not enabling for any of the innumerable number of SCP variant peptides currently encompassed in the scope of instant claims. Applicants have not enabled the full scope of the invention as claimed broadly. For these reasons, making and using of the instantly claimed peptide variant(s), which has the desired function(s) is well outside the realm of routine experimentation. The claims are viewed as being non-enabled with regard to the full scope. Accordingly, undue experimentation would have been required by one of ordinary skill in the art at the time of the effective filing date of the instant application to reproducibly practice the invention as claimed due to the lack of specific guidance, the lack of disclosure enabling the full scope, the art-demonstrated unpredictability

associated with the structure-function relationship with a polynucleotide or polypeptide, the art-demonstrated unpredictability in determining amino acid variations that are acceptable, the breadth of the claims, and the quantity of experimentation necessary. *Ex parte Foreman, 230 USPQ 546, 547 (Bd. Pat. Appls. And Interf. 1986)*. Instant claims are viewed as not meeting the scope of enablement provisions of 35 U.S.C § 112, first paragraph.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

13) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

14) Claims 60-72 and 75-78 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, which Applicants regard as the invention.

(a) Claims 60-65, 67, 68, 70, 71 and 75-78 are vague and confusing in the use of an abbreviation in the claim language: 'SCP'. It is suggested that the abbreviation be recited as a full terminology in the base claim with its abbreviation retained within parentheses.

(b) Claim 61 has improper antecedence in the limitation: 'of claim 60 wherein the vaccine' (see line 1), because claim 1 is not directed to a 'vaccine'.

(c) Claim 61 is vague and indefinite in the recitation 'variant', because it is unclear what is encompassed in this limitation. What constitutes a 'variant' and how much of the streptococcal C5a peptidase's original structure has to be retained such that the resulting peptide can be considered as a 'variant' is not clear. The metes and bounds of the structure encompassed in the limitation 'variant' are indeterminate.

(d) Claims 65 and 66 have improper antecedence in the limitation 'of claim 64 wherein the DNA' (see line 1), because claim 64 does not recite any 'DNA'. Claim 63 from which claim 64 depends does not recite any 'DNA' either.

(e) Claim 65, which depends from claim 64, is vague and indefinite in the recitation 'DNA encodes an SCP'. Since the recitation lacks antecedence, it is unclear whether this is a different SCP than what is recited in claim 64.

(f) Claims 65, 66, 68 and 69 are confusing, because the claims are drawn to a peptide, yet the claims include the confusing recitation 'wherein the DNA encodes'. Are the claims intended to be directed to the DNA or the peptide?

(g) Claims 65, 66 and 68-72 are vague and indefinite in the recitation of one or more amino acid residues, such as 260, 261 262, 415, 130-512 etc. without identifying the claimed peptide by its SEQ ID

number. The metes and bounds of the instant claims are indeterminate because it is unclear which amino acid in the claimed peptide is to be considered, for example, as the amino acid residue 130, 295 or 512 etc. How one would determine a particular amino acid residue to be the residue at 130 or 512 etc. is not clear. In order to effect a substitution or modification at position 512 as recited in claims 70 and 71, one needs to know which amino acid is the amino acid residue at position 512, for which one needs to know whether the numbering starts after the signal sequence or before the signal sequence and in a full length polypeptide or a truncated peptide. Without the identification of the peptide in the claims by a specific SEQ ID number, one cannot envision the scope and length of the claimed product, or the position(s) of the recited amino acids.

(h) Claim 60 is vague, indefinite and confusing in the phrase: 'peptide comprising ..... SCP'. It is unclear how a 'peptide' (which is generally shorter than a polypeptide or protein) can comprise 'SCP' which appears to be an enzyme protein.

Rejection(s) under 35 U.S.C. § 102

15) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> **(e)** The invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.
> **(f)** he did not himself invent the subject matter sought to be patented.

16) Claims 60, 77 and 78 are rejected under 35 U.S.C. 102(f) because Applicants did not invent the claimed subject matter. Claims 1 and 5 of US patent 5,846,547 ('547 – Applicants' IDS) encompass an enzymatically inactive streptococcal C5a peptidase (SCP), but had only Cleary as the sole inventor. The instant specification presents claims to a peptide comprising the same SCP peptidase, however lists Cleary and Stafslien as the inventors. It does not appear that the instant inventors invented the subject matter sought to be patented in the instant application.

17) Claim 60 is rejected under 35 U.S.C. § 102(b) as being anticipated by Cleary *et al.* (US 4,772,584 – Applicants' IDS) ('584).

It is noted that the claimed peptide encompasses 'a portion of a full-length protein' or a truncated fragment of the protein.

Cleary *et al.* ('584) disclosed an isolated and purified enzymatically hydrolysed streptococcal SCFI, a C5a chemotaxin-inhibitor, which gave rise to some cleavage peptide products having their biological activity, i.e., enzymatic activity, eliminated (see column 8, lines 19-24 and Examples). Cleary's ('584) product anticipated the instantly claimed product.

Claim 60 is anticipated by Cleary *et al.* ('584).

18) Claims 60-62 and 75-78 are rejected under 35 U.S.C § 102(e) as being anticipated by Green *et al.* (US 6,100,380, filed 06/07/1995) as evidenced by *The Concise Encyclopedia: Biochemistry and Moelcular Biology* (Third Edition, (Ed) Scott TA *et al.*, Walter de Gruyter, New York, p. 489, 1997).

It is noted that the claimed peptide is neither identified in the claim(s) by its structure or SEQ ID number, or by its molecular weight.

The term 'peptide' in the instant claim(s) is given the art known definition, i.e., an organic compound consisting of two or more amino acids joined covalently by peptide bonds. See page 489 of *The Concise Encyclopedia: Biochemistry and Moelcular Biology* Third Edition, (Ed) Scott TA *et al.*, Walter de Gruyter, New York, 1997.

The transitional limitation "comprising" similar to the limitations, such as, "having", "including," "containing," or "characterized by" represents open-ended claim language and therefore does not exclude additional, unrecited elements. See M.P.E.P 2111.03 [R-1]. See *Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986)*; *In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981)*; *Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)* ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts"). On the other hand, the limitation "consisting of" represents closed claim language and excludes any element, step, or ingredient not specified in the claim. *In re Gray, 53 F.2d 520, 11 USPQ 255 (CCPA 1931)*; *Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)*.

Green *et al.* disclosed an isolated Gly-Lys dipeptide. A therapeutic or prophylactic preparation comprising the dipeptide in saline for *in vivo* administration (see abstract and Example 7) suggests that the peptide is present in a sufficiently purified form. The prior art Gly-Lys dipeptide constitutes a peptide of the amino acid sequence depicted in Figure 2 for SCP from group A streptococcal serotype 49 (see positions 119 and 120 of SEQ ID NO: 1 in Figure 2). Such a short two amino acid-containing peptide of the prior art serves as a truncated variant of the SCP and is expected by those of skill in the art not to be enzymatically active and not to bind with the same intensity as the wild-type SCP. The enzymatic inactivity and reduced binding activity compared to the native SCP are viewed as inherent properties inseparable from the prior art dipeptide variant, absent evidence to the contrary.

The limitation 'expressed from an isolated DNA sequence encoding SCP' in claim 62 is a process limitation in a product claim. The product-by-process claims are not limited to the manipulations of the recited steps, but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a

> different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art bacterial strain differs from that of the instantly claimed bacterial strain. The prior art product meets the instant claims and anticipates the claimed product.

Claims 60-62 and 75-78 are anticipated by Green *et al.*

19) Claims 60-69 are rejected under 35 U.S.C. § 102(b) as being anticipated by Wexler *et al.* (*PNAS* 82: 8144-8148, 1985 – Applicants' IDS).

Wexler *et al.* taught an isolated and purified C5a inactivating streptococcal SCFI enzyme (i.e., SCP) wherein the activity (i.e, enzymatic activity) has been neutralized or terminated using SCFI-specific antiserum (see abstract; page 8144, right column; and page 814, left column). That an antiserum-neutralized SCFI enzyme serves as a varied molecule and has reduced binding activity compared to the native SCFI is inherent from the teachings of Wexler *et al.* Since Wexler's SCFI is a whole molecule produced by the natural encoding of a DNA from a group A streptococcus, it inherently contains every part of the full length SCP molecule, including a specificity crevice or a catalytic domain; contiguous amino acid residues from about residue 260-417; one or more amino acid residues130, 193, 260, 261, 262, 295, 415, 416, 417 or 512.

The phrase 'expressed from an isolated NDA sequence encoding SCP' is a process limitation in a product claim. The product-by-process claims are not limited to the manipulations of the recited steps, but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art bacterial strain differs from that of the instantly claimed bacterial strain. The prior art product meets the instant claims and anticipates the claimed product.

Claims 60-69 are anticipated by Wexler *et al.*

Remarks

20) Claims 60-72 and 75-78 stand rejected.

21) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives papers 24 hours a day and seven days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

22) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.45 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

March, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER